REMARKS

Claims 20-41 and 43-46, are pending in this application. Claims 31, 34-38, 45 and 46, have been withdrawn from consideration, as being drawn to a non-elected invention.

Claim 42 has been canceled without prejudice or disclaimer.

Claims 20, 25, 26, 32, and 33, have been amended to clearly set forth that the antigenic protein is secreted extracellularly, and to require ligation "such that said antigenic protein is secreted extracellularly".

Claims 29, 30, 41, 43 and 44, have been amended to more clearly define the invention.

Claims 26 and 33 have been amended to positively recite that the "...fusion protein upon administration into a host cell, immunizes said host cell against subsequent infection with *Mycoplasma gallisepticum*...."

Support for the claims as amended, appears throughout the specification, Example 1, the sequence listings, and the claims, as originally filed. Please see pages 8, 10 and 14, of the present specification. No new matter has been added.

In view of the amendments to the claims and the remarks set forth below, further and favorable consideration is respectfully requested.

I. At page 2 of the Final Office Action, the Examiner states that claims 31, 34-38 and 45-46, are withdrawn from consideration as being directed to a non-elected invention.

The Examiner states that Applicant's constructively elected claims 27-30, 32-33 and 39-44 because of claims originally presented.

Applicant's submit that claims 45 and 46 should be examined with claims 27-30, 32-33 and 39-44 because claims 45 and 46 are directed to a recombinant live vaccine and are dependent on pending claim 26. Thus, it is submitted that claims 45 and 46 are not directed to a product that is different and/or distinct from the elected/pending claims.

Further, the Examiner states that "Newly submitted claims 31, 34-38 and 45-46 are directed to an invention that is independent or distinct form the invention originally claimed..." Applicant's note that original claim 9 is directed to "A hybrid DNA coding for a fusion protein..." Accordingly, it is submitted that the subject matter of claims 31 and claims dependent therefrom (34-38), is not independent or distinct from the invention originally claimed.

In view of the foregoing, it is submitted that restriction of the claims is improper, and that claims 31, 34-38 and 45-46 should properly be examined. Accordingly, examination of claims 31, 34-38 and 45-46, is respectfully requested.

I. At page 3 of the Final Office Action, the Examiner maintains the rejection of claims 20-24 and 29-30, and newly rejects claims 41-42, under 35 USC § 103 (a) as being unpatentable over Saito (WO 94/23019) in view of Yoshida (Virology 1994, Vol. 200).

A. The Rejection:

The Examiner maintains that it would have been obvious to the skilled artisan to use the herpes virus outer membrane polypeptide derived from Yoshida et al. with the fusion protein including an outer membrane protein that infects birds and vaccine of Saito because Yoshida teaches that the FPV recombinant express the gB-1 gene which can elicit neutralizing antibody and fully protect chickens against challenge with virulent strains of MDV; the FPV recombinant is a good candidate for an MDV vaccine; and that gB is an important target for the host immune response.

The Examiner's response to Applicant's arguments presented April 10, 2003:

1. ***Motivation to combine:*** The Examiner states that applicants argument that the lack of *in vivo* results in Saito are the reason why a skilled artisan would not use the Saito disclosure to prepare a hybrid fusion protein or recombinant virus with a view to preparing a live vaccine, is unpersuasive because, a patent is relevant as prior art for all it contains. The Examiner points to **MPEP 2123.**

2. ***In vivo activity, functional limitation:*** The Examiner states that the functional limitation of *in vivo* activity does not result in a structural difference and that if the prior art structure is capable of performing the intended use, then it meets the claim.

3. ***Teaching away:*** The Examiner states that: **(a)** applicant's arguments regarding *teaching away* are not persuasive because the prior art disclosed examples and preferred embodiments do not constitute a *teaching away* from a broader disclosure or non-preferred embodiment, and **(b)** that applicant's arguments regarding the membrane anchoring sequence are unpersuasive because the instant claims recite "comprising" and do not exclude a membrane anchor sequence.

4. ***Motivation to combine:*** Regarding applicant's arguments as to lack of motivation to combine references, the Examiner states that only routine skill is necessary to use the signal polypeptide derived Herpes protein from Yoshida with Saito and that one of ordinary skill in the art would have a reasonable expectation of success. The Examiner states that the use of a functionally equivalent technique or component would have been desirable to the skilled artisan.

B. The Present Invention:

Claim 42 has been canceled without prejudice or disclaimer. Claims 20, 25, 26, 32, and 33, have been amended to require ligation of sequences and/or polypeptides "such that said antigenic protein is secreted extracellularly" and to require "wherein upon expression of said fusion protein in a host cell, said antigenic protein is secreted extracellularly". Claims 21-24 and 29 are directly or indirectly dependent on amended claim 20. Claim 41 is dependent on claim 32. Support for the claims as amended, appears throughout the specification, Example 1, the sequence listings, and the claims, as originally filed. No new matter has been added.

Claims 26 and 33 have been amended to positively require that "said fusion protein upon administration into a host cell, immunizes said host cell against subsequent infection with..."

Claims 29, 30 and 41, requires that the antigenic protein causes an antigen-antibody reaction *in vivo*.

Claim 41 is dependent on independent claim 32. It is noted that the Examiner has not rejected claim 32.

C. The Applied Art:

Saito, US Pat. No: 5,871,742:

Saito teaches a recombinant Avipox virus encoding a polypeptide of Mycoplasma gallisepticum, and a live vaccine. Saito requires a fused polypeptide including the antigenic Mycoplasma gallisepticum polypeptide and a signal membrane anchor of a type II outer-membrane

polypeptide of a virus that infects birds, which includes a membrane anchoring sequence and a signal sequence. Saito does not teach a polypeptide derived from a Herpes outer membrane protein. Saito report deficient *in vivo* results.

Yoshida:

Yoshida teaches an FPV recombinant that expresses the entire gB-1 gene including the signal, anchor and coding sequences, and indicates that the FPV recombinant is a good candidate for a MDV vaccine and that gB is an important target for the host immune response. Yoshida requires insertion of the full length of gB, including its signal sequence and its membrane anchoring sequence, into FPV.

D. In View of the Following, this Rejection is Respectfully Traversed:

It is submitted that a proper case of *prima facie* obviousness has not been established. The combination of Saito and Yoshida is improper, because there is no motivation or suggestion supporting the combination. Assuming *arguendo* the combination proper, there is no motivation to modify Yoshida and/or Saito by ligating the signal sequence of Yoshida with the antigen gene sequence of Saito, such that the antigenic protein is secreted extracellularly, as presently required.

(i) Authority:

(a) Motivation to combine references:

MPEP 2143 discusses the requirements of a *prima facie* case of obviousness. First there must be some suggestion or motivation to combine the reference teachings or to modify the

reference, and second there must be a reasonable expectation of success. Finally, the prior art reference or references when properly combined, must teach or suggest all the claim limitations.

MPEP 2143.01 states that there are three possible sources for a motivation to combine references: the nature of the problem being solved, the teachings of the prior art, and the knowledge of one of ordinary skill in the art. Further, **MPEP 2145 (X)(D)(2)** states that "It is improper to combine references where the references *teach away* from their combination."

This section quotes *In re Grasselli*, 713 F.2d 731 (Fed. Cir. 1983) which court held that a claimed catalyst which contained both iron and an alkali metal was not suggested by the combination of a reference which taught the interchangeability of antimony and alkali metal with the same beneficial result, combined with a reference expressly excluding antimony from , and adding iron to, a catalyst.

A combination of references may teach every element of a claimed invention, but without a motivation to combine the references, a rejection based on a *prima facie* case of obvious was held improper. *In re Rouffet*, 149 F.3d 1350 (Fed. Cir. 1998).

(b) Motivation to modify properly combined references:

Further, where the prior art conflicts, all teachings must be considered. The fact that references can be combined or modified is not sufficient to establish *prima facie* obviousness. **MPEP 2143**.

MPEP 2143 states that there must be some suggestion or motivation to modify the

references, and there must be a reasonable expectation of success. Finally, the prior art reference or references when properly combined, must teach or suggest all the claim limitations.

MPEP 2143.01 states that a proposed modification cannot render the prior art unsatisfactory for its intended purpose. If it does, then there is no suggestion or motivation to make the proposed modification. Further, the proposed modification cannot change the principle operation of a reference.

Regarding combining references, the court in *In re Oetiker,* 977 F.2d 1443 (Fed. Cir. 1992), held that "There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the combination. That knowledge can not come from the applicant's invention itself." The court in *In re Paulsen,* 30 F.3d 1475 (Fed. Cir. 1994), held "in reviewing the Board's obviousness conclusions, we have been guided by the well-settled principles that the claimed invention must be considered as a whole, multiple cited prior art references must suggest the desirability of being combined, and the references must be viewed without the benefit of hindsight afforded by the disclosure."

The court in *In re Rouffet,* 149 F.3d 1350 (Fed. Cir. 1998), held that "...this court requires the examiner to show a motivation to combine the references that create the case of obviousness...there must be some teaching, suggestion, or motivation to combine the references....three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art."

The court in *Winner International Royalty Corp. v. Wang*, 202 F.3d 1340 (Fed. Cir. 2000), held that if a prior art reference "did in fact teach away from [a second reference], then that finding alone can defeat [an] obviousness claim" based on combination of the two references. In *Karsten Manufacturing Corp. v. Cleveland Golf Co.*, 242 F.3d 1376 (Fed.Cir. 2001), the court held that "the conflicting teachings of two prior art references can not reasonably be viewed as suggesting their combination..."

(c) Teaching away:

MPEP 2141.02 states that prior art must be considered in its entirety, including disclosures that *teach away* from the claims. See also **MPEP 2145 (X)(D).**

The court in *In re Gurley,* 27 F.3d 551 (Fed. Cir. 1994) held that "A prior art reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." The court in *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.,* 796 F.2d 443 (Fed. Cir. 1986), held that "A reference should be considered as a whole, and portions arguing against or teaching away from the claimed invention must be considered."

(d) Obvious to try:

Obvious to try is not the proper standard for patentability. The court in *In re Lilly & Co.,* 902 F.2d 943 (Fed. Cir. 1990), held that an "obvious-to-try" situation exists when a general disclosure

may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued."

The court in *In re O'Farrell,* 853 F.2d 894 (Fed. Cir.1988), held that the admonition that obvious-to-try is not the standard under section 103 has been directed at two kinds of errors, (i) where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful, and (ii) where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it, that is what was obvious-to-try was to explore a new technology or general approach that seemed to be a promising field of experimentation. See also **MPEP 2145 XB.**

(ii) Applicant's Response to Examiner's remarks:

All of the pending claims require ligation such that the antigenic protein is secreted extracellularly, and require that upon expression of the fusion protein in a host cell, the antigenic protein is secreted extracellularly.

(a) ***Motivation to combine:*** At page 3 of the Final Office Action the Examiner states that **MPEP 2123** teaches that patents are relevant as prior art for all they contain. The Examiner further states that "...The court held that the prior art anticipated the claims even though it taught away from the claimed invention..." The Examiner follows this quote with "Therefore applicant's argument is not persuasive especially when considering the prior art teaches the use of the same antigenic

...protein and a signal polypeptide of the outer membrane protein comprised as a fusion protein..."

The instant rejection is under 35 USC § 103, NOT 35 USC § 102. Accordingly, the Examiner's position that a court found that a prior art reference anticipated claims and also taught away from those claims, is irrelevant. If claims are found to be anticipated, the question of whether or not they are obvious, does not arise. The subject quote indicates if anything, that the claims were anticipated ***and*** unobvious. In support of the foregoing, the court in *Celeritas Tech, Ltd. v. Rockwell,* 150 F.3d 1354 (Fed. Cir. 1998), held that the question of whether a reference "teaches away" from the invention is inapplicable to an anticipation analysis.

The Examiner's conclusion, i.e., "Therefore applicant's argument is not persuasive....", assumes that a *prima facie* case of obviousness has been established, i.e., that the references are properly combined. Applicant's argument is that there is no motivation or suggestion supporting the combination of Saito with Yoshida, and therefore a case of *prima facie* obviousness has not been established.

The inquiry as to whether proper motivation to combine exists, is discussed in **MPEP 2143** which states the requirements of a *prima facie* case of obviousness, i.e., there must be some suggestion or motivation to combine the reference teachings, and that there are three possible sources for a motivation to combine references: the nature of the problem being solved, the teachings of the prior art, and the knowledge of one of ordinary skill in the art. **MPEP 2145 (X)(D)(2)** states that "It is improper to combine references where the references *teach away* from their combination." In

determining whether a combination is proper, only the references themselves are considered, ***not*** the presently claimed invention.

In the present case, Saito reports deficient *in vivo* results are achieved. Yoshida discloses that the FPV recombinant including the full length of the gB sequence (i.e., signal, anchor and antigenic sequence), expresses the gB-1 gene, and indicates that an FPV recombinant is a good candidate for a MDV vaccine. Accordingly, the skilled artisan in view of Saito's teaching of deficient *in vivo* results, would have ***no*** motivation to look to Saito in order to produce a vaccine with good *in vivo* activity ***because Saito reports deficient in vivo activity.*** See **MPEP 2143**.

The Examiner states at page 4 of the Final Office Action, that the functional limitation of *in vivo* activity does not result in a structural difference and that if the prior art structure is capable of performing the intended use, then it meets the claim. Again, the argument, as stated at page 19, lines 1-3 of the Amendment filed on April 10, 2003, is that the ***combination of references is improper because the skilled artisan in view of Yoshida would have no motivation to look to prior art that reports deficient in vivo results (Saito).***

The Examiner states at page 6 and 7 of the Final Office Action, that applicant's arguments as to lack of motivation to combine references are unpersuasive because only routine skill is necessary to use the signal polypeptide derived Herpes protein from Yoshida with Saito and that one of ordinary skill in the art would have a reasonable expectation of success. The Examiner states that the use of a functionally equivalent technique or component would have been desirable to the skilled

artisan based on prior use and well-known advantages of such compositions and vaccines based on the ease and availability of the components.

The Examiner's statement that "...only routine skill is necessary...", does not constitute motivation to combine the references, let alone motivation sufficient to support the combination.

Again, the instant argument and the arguments previously presented, are directed to whether ***the combination of references is proper***, not whether properly combined references suggest the claimed invention. Please see **MPEP 2141.02.**

In view of the above, it is submitted that the combination of Saito with Yoshida, is improper. Accordingly, it is submitted that a proper case of *prima facie* obviousness has not been established. Thus, the Examiner is respectfully requested to withdraw this rejection.

(b) ***Motivation to modify properly combined references:*** Assuming *arguendo* the combination proper, it is submitted that the skilled artisan would have not motivation to modify Saito and/or Yoshida, in order to obtain the present invention.

Teaching away: The Examiner states at pages 4 and 5 of the Final Office Action, that applicant's arguments regarding *teaching away* are not persuasive because the prior art disclosed examples and preferred embodiments do not constitute a *teaching away* from a broader disclosure or non-preferred embodiment, and that applicant's arguments regarding the membrane anchoring sequence are unpersuasive because the instant claims recite "comprising" and are thus open-ended, i.e., do not exclude a membrane anchor sequence.

The accepted standard regarding "teaching away" is set forth in *In re Gurley,* 27 F.3d 551 (Fed. Cir. 1991), which court held that "A prior art reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, ..."

In the present case, Saito ***teaches away*** from producing a recombinant Avipox virus, because Saito teaches **deficient** *in vivo* results. ***Such deficient results would discourage the skilled artisan from following Saito's path***. Accordingly, there is no motivation to modify Saito, in order to obtain the claimed invention. Further, the Examiner must consider Saito in it's entirety including portions that *teach away*.

In addition, Yoshida ***teaches away*** from producing an antigenic protein that is secreted extracellularly, because Yoshida teaches at page 491, second full paragraph, that HSV gB is ***anchored by the trans-membrane domain*** and that "...the trans-membrane domain is not only involved in membrane anchoring, ***but is also required*** for intracellular transport and localization." Thus, the skilled artisan would have no motivation to remove the membrane anchor sequence to produce a secreted antigenic protein, because Yoshida teaches that such removal interferes with proper processing and transport of the antigenic protein. That is, the skilled artisan in view of Yoshida, ***would be discouraged from producing an antigenic protein that is secreted extracellularly***, because Yoshida teaches the expression of a protein where the protein is bound at the cell surface via the trans-membrane domain encoded by the anchor sequence and that this trans-

membrane is ***necessary for proper processing and transport.***

All of the rejected claims require that the sequences/polypeptides be ligated such that the antigenic protein is secreted extracellularly, and require that upon expression of the fusion protein in a host cell, the antigenic protein is secreted extracellularly.

Neither Yoshida nor Saito teach or suggest a sequence encoding a fusion protein, or a fusion protein, or a recombinant live vaccine including DNA encoding the fusion protein, or a recombinant Avipox virus including such DNA, where the sequences/polypeptides are ligated such that the antigenic protein is secreted extracellularly, and where upon expression of the fusion protein in a host cell, the antigenic protein is secreted extracellularly, as presently required. Both of Yoshida and Saito teach constructs where the antigenic protein is expressed at the cell surface and is bound to the surface via the membrane anchor peptide.

Regarding the Examiner's position that the present claims recite the transition term "comprising" and thus do not exclude a membrane anchor sequence, Applicant's note that the present claims ***require*** that the antigenic protein be secreted extracellularly. It is not necessary to expressly exclude a membrane anchor sequence, because the claims exclude any construct ligated to the antigenic protein/sequence that does not result, upon expression of the fusion protein in a host cell, in extracelllular secretion of the antigenic protein.

MPEP 2173.05 (g) discusses function language in claims, and quotes *In re Barr,* 444 F.2d 588 (CCPA 1971) which court held that the limitation (used to define a chemical compound)

"incapable of forming" a dye, although functional, was perfectly acceptable because it set definite boundaries on the patent protection sought. Likewise, in the present case, the functional limitation, i.e. the requirement of extracellular secretion, set definite boundaries, and is acceptable.

Saito ***requires*** a fused polypeptide including the antigenic Mycoplasma gallisepticum polypeptide and a signal membrane anchor of type II outer-membrane polypeptide of a virus that infects birds, which is encoded by *a membrane anchoring sequence* which is directly ligated to a signal sequence where the expressed antigenic protein is bound to the surface via the membrane anchor. Thus, Saito provides no motivation or suggestion, to modify Yoshida to produce an antigenic protein that is secreted extracellularly, as presently required.

Yoshida ***requires*** an FPV recombinant that ***expresses*** the ***entire*** gB-1 gene including the signal, anchor and coding sequences, and requires insertion of the full length of gB including its signal sequence directly ligated to its membrane anchoring sequence, into FPV where the antigenic protein is bound at the cell surface via the membrane anchor. Thus, Yoshida provides no motivation or suggestion, to modify Saito to produce a protein that is secreted extracellularly, as presently required.

In further support of the foregoing, Yoshida requires the entire gB gene including signal, anchor and coding sequences; Yoshida requires the gB antigen gene and does not suggest any other antigen or disease state; and Yoshida does not suggest using the signal and anchor gB sequence separate from the coding sequence. Thus, there is no motivation to modify Yoshida by ligating the

signal/anchor sequence of Yoshida with the antigen gene sequence of Saito. Yoshida does not provide any guidance or direction on how such sequences could be accomplished. Yoshida does not teach a herpes virus outer membrane polypeptide absent the antigenic peptide.

Lastly, neither Saito nor Yoshida teach or suggest a construct absent a membrane anchor sequence or a construct where a membrane anchor sequence is not directly ligated to an antigenic sequence, such that extracellular secretion of the antigenic protein is achieved.

More specifically, the combination (assuming *arguendo* the combination proper), at most, suggests ligating the Herpes virus outer membrane sequence including the signal and membrane anchor sequences, with the antigenic sequence of Saito, such that the antigenic protein is expressed at the host cell surface and is bound to the surface via the membrane anchor peptide.

In view of the above, it is submitted that a *prima facie* case of obviousness has not been established, and that the combination of Saito and Yoshida, establishes at most, that the present invention may have been "obvious to try". "Obvious to try" is not the proper standard for patentability. Please see *In re O'Farrell, supra.* Neither reference, taken alone or together, provides any guidance of how to obtain the presently claimed invention. See also *In re Lilly & Co., supra.*

In conclusion, neither of Yoshida or Saito provide any motivation to modify their respective recombinants in order to produce the presently claimed fusion protein, vaccine or virus, where the

antigenic protein is secreted extracellularly. Neither of Yoshida or Saito teach extracellular secretion and both require a membrane anchor sequence directly ligated to the signal sequence such that the expressed protein is bound at the cell surface. Please see **MPEP 2143** (motivation to modify) and **MPEP 2141.02** and **MPEP 2145 (X)(D)** (teaching away).

Further, if Yoshida and/or Saito were modified to produce an antigenic protein that is secreted extracellularly, then that modification would render Yoshida and/or Saito unsatisfactory for their respective intended purposes. Again, both Yoshida and Saito teach that the protein is bound via the membrane anchor peptide, at the cell surface. Further, Yoshida requires that the membrane anchor sequence be present in order to ensure proper protein processing. Please see **MPEP 2143.01.**

Further, such a modification would change the principal operation of the references, because both references require a membrane anchor sequence directly ligated to the signal sequence resulting in an antigenic protein that is not secreted, and is bound at the cell surface. Again, please see **MPEP 2143.01**, which states that if the proposed modification renders the prior art unsatisfactory for its intended purpose or changes the principal operation of reference, then there is no suggestion or motivation to make the proposed modification. Thus, there is no suggestion or motivation to make the modification proposed by the Examiner.

In view of the amendments to the claims and the remarks set forth above, it is submitted that nothing in Saito and Yoshida, taken alone or together, renders the claimed invention obvious within

the meaning of 35 USC § 103. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

In further support of the unobviousness of the present invention, attached hereto please find Exhibit B which was submitted to the Examiner together with the Amendment filed on April 10, 2003.

As clearly illustrated in Exhibit B, neither Saito nor Yoshida teach or suggest an antigenic protein that is secreted extracellularly.

More specifically, as seen from Exhibit B, in the methods of both Saito and Ysohida, the membrane anchor peptide is directly ligated with the antigenic peptide, where a signal peptide is also used. Therefore, the antigenic peptide is expressed and exposed on the cell membrane, but it is not secreted extracellularly due to the existence of the membrane anchor peptide directly ligated with the antigenic protein.

On the other hand, as seen from Exhibit B, in the present invention, the antigenic peptide is ligated with the signal peptide at the N terminus thereof, and the membrane anchor peptide is not essential for the present invention.

Thus, the present invention does not require the membrane anchor peptide, although the anchor peptide may be present provided it is ligated such that extracellular secretion of the antigenic protein occurs, i.e., provided that expression of the membrane anchor sequence does not result in the antigenic protein being bound at the cell surface.

Yohishida and Saito both ***require*** a membrane anchor sequence which is ***directly*** ligated to the signal sequence thus resulting in the expressed protein being bound at the cell surface, i.e., both require that the membrane anchor sequence be ***functional***, i.e., ligated to the signal sequence such that the expressed protein is bound at the cell surface. Please see Yoshida, Saito, and Exhibit B filed herewith.

The present claims ***require*** extracellular secretion of the antigenic protein. How secretion is accomplished is irrelevant. In the present invention, it is necessary that the antigenic protein and the signal polypeptide be ligated at the N terminus of the protein such that the antigenic protein is secreted extracellularly. It is ***inherent*** that there is a structural difference between a fusion protein or DNA encoding such protein, which results in extracellular secretion of an antigenic protein, and a fusion protein or DNA encoding such which results in an expressed antigenic protein that is bound at the cell surface via a membrane anchor peptide.

Accordingly, neither of Yoshida or Saito, teach or suggest extracellular secretion or a construct (fusion protein, DNA, virus) which produces a secreted antigenic protein, as presently required.

In view of the above and the amendments to the claims, it is submitted that nothing in Yoshida or Saito, taken alone or together, render the claimed invention obvious within the meaning of 35 USC § 103. Thus, the Examiner is respectfully requested to withdraw this rejection.

IV. At page 8, paragraph 5, of the Final Office Action, the Examiner maintains the rejection of claims 25-26 and 32-33 under 35 USC § 103 (a) as being unpatentable over Saito (WO 94/23019) in view of Yoshida (Virology 1994, Vol. 200) and further in view of Yangida.

The Examiner contends that it would have been obvious to use the recombinant Avipox virus with exogenous DNA as taught by Yangida et al, with the fusion polypeptide of Saito et al., in view of Yoshida et al., because Yangida et al. teach that recombinant Avipox virus genes are effective as vaccines and can prevent infections of Avipox virus.

The rejected claims are directed to a recombinant Avipox virus or live vaccine, and all require that the sequences/polypeptides are ligated such that the antigenic protein is expressed extracellularly. Claims 26 and 33, further require that the fusion protein upon administration into a host cell, immunizes the host cell against subsequent infection with Mg.

In view of the above discussions regarding the previous rejection, it is submitted that the combination of Saito and Yoshida is improper; assuming *arguendo* the combination proper, that there is no motivation to modify Yoshida and/or Saito; and that Yangida does not cure the deficiencies of Saito or Yoshida, taken alone or together.

Please see the above arguments.

Yangida does not cure the deficiencies of Saito and Yoshida, because Yangida also does not suggest the present virus/vaccine where the sequences/polypeptides are ligated such that the antigenic protein is expressed extracellularly, as required by present claims 25-26 and 32-33. Further, Yangida does not suggest a vaccine where the sequences/polypeptides are ligated such that

the antigenic protein is expressed extracellularly, where the fusion protein upon administration into a host cell, immunizes the host cell against subsequent infection with Mg, as required by present claims 26 and 33.

In view of the foregoing and the amendments to the claims, it is submitted that nothing in Yoshida , Saito and/or Yangida, taken alone or together, render the claimed invention obvious within the meaning of 35 USC § 103. Thus, the Examiner is respectfully requested to withdraw this rejection.

V. At page 9, paragraph 6, of the Final Office Action, claims 25-26, 32-33, and 40-44, have been rejected under 35 USC 112, 1st paragraph, as containing new matter.

The Examiner states that neither the specification or the original claims provide support for a recombinant Avipox virus or recombinant live vaccine: **(a)** with the ability to secrete the antigenic protein extracellularly, **(b)** outside the cell, **(c)** at the surface of the cell and **(d)** does not contain a membrane anchor sequence. The Examiner states that pages 8 and 10 fail to provide such support.

Claim 42 has been canceled without prejudice or disclaimer. All of the claims require that the antigenic protein is secreted extracellularly. None of the claims require expression "outside the cell" or "at the surface of the cell".

MPEP 2163.05 addresses ***changes to the scope of claims***, and recites "...To comply with the written description requirement...each claim limitation must be expressly, ***implicitly***, or ***inherently***

supported in the originally filed disclosure..." (Emphasis added). The Federal Circuit has consistently held that *ipsis verbis* disclosure is ***not necessary*** to satisfy the written description requirement. Instead, the disclosure need only reasonably convey to the skilled artisan that the inventor had possession of the subject matter in question. See *In re Wilder*, 736 F.2d 1516 (Fed. Cir. 1984); *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570 (Fed. Cir. 1985); and *Fujikawa v. Wattanasin*, 93 F.3d 1559 (Fed. Cir. 1996). See also **MPEP 2163.06.**

Further, **MPEP 2163.07 (a)** states that by disclosing in a patent application a device that inherently performs a function or has a property, or operates according to a theory or has an advantage, a patent application necessarily discloses that function, theory or advantage, even though it says nothing explicit concerning it. The application may later be amended to recite the function, theory or advantage without introducing prohibited new matter.

The present specification teaches at page 5, lines 4-19, that the invention provides "a fusion protein...*a polypeptide **derived** from the outer membrane protein of a herpes virus*..."; "a hybrid DNA coding for the fusion protein; a recombinant Avipox virus in which the hybrid DNA as been incorporated; and, a live vaccine comprising the Avipox virus as an effective ingredient."

The present specification teaches at page 8, lines 8-16, that "The Herpesvirus-derived polypeptides may not always be the full length of the proteins....and where the polypeptides are employed for secretion, the polypeptides ***may contain only a signal sequence*** for that purpose." This passage expressly supports the present embodiments **(b)** and **(d)** above where the antigenic

protein is secreted extracellularly and where the protein does not include a membrane anchor sequence.

Page 10 of the present specification, at lines 2-12, states that the outer membrane protein (which includes the signal sequence and the membrane anchor sequence) are digested and the resulting fragements which are "DNA fragment coding for the outer membrane protein of herpes viruses or for the signal sequence of the outer membrane protein..." are ligated with the DNA fragment coding for the antigen protein. This passage clearly supports the present embodiments **(b)** and **(d)** above where the antigenic protein is secreted extracellularly and where the protein does not include a membrane anchor sequence.

Page 10, paragraph 2, states that a fusion protein of the invention includes the protein represented by Sequence ID No: 2 which includes only a signal sequence (a.a. 1-63) and an antigenic protein sequence (a.a. 64-456), and not a membrane anchor sequence. Likewise, Sequence ID No: 1 (see also page 28) is the nucleotide sequence coding for the fusion protein of Sequence ID No: 2 (see also page 32). Again, this clearly supports the present embodiments **(b)** and **(d)** above where the antigenic protein is secreted extracellularly and where the protein does not include a membrane anchor sequence. It is noted that the present specification states that when secretion is desired, only the signal sequence needs to be included. Further, it is inherent that a construct of the noted Sequence ID's result in extracellular secretion of the antigenic protein, because a membrane anchor sequence is not present.

Page 11 of the specification describes a recombinant Avipox virus including the noted DNA.

Page 14, paragraph 3, describes a live vaccine prepared using the noted virus.

Page 27 of the specification, states that "... the hybrid DNA's can secrete the antigenic proteins extracellularly to obtain Avipox viruses that can be efficiently recognized by the antigen recognizing cell in host cells and that the thus obtained recombinant Avipox viruses are useful as potent vaccines for anti-Mycoplasma infection."

In view of the foregoing, it is submitted that the present claims including claim limitations, are expressly, implicitly and inherently, described in the present specification, examples, figures and claims as originally filed, sufficient to reasonably convey to the skilled artisan that the inventor had possession of the subject matter in question.

In view of the above and the amendments to the claims, it is submitted that presently claimed invention is fully supported by the specification, examples and claims as originally filed, within the meaning of 35 USC § 112. It is submitted that none of the claims contain new matter. Accordingly, the Examiner is respectfully requested to withdraw this rejection. Clarification is respectfully requested if this rejection is to be maintained.

It is submitted that the present claims are in condition for immediate allowance, and early notice to that effect is earnestly solicited.

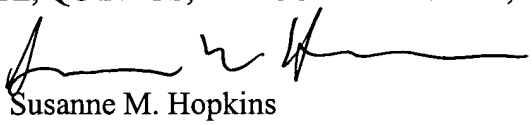
If, for any reason, it is felt that this application is not now in condition for allowance, the

Examiner is requested to contact Applicants undersigned attorney at the telephone number indicated below to arrange for an interview to expedite the disposition of this case.

In the event that this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. Please charge any fees for such an extension of time and any other fees which may be due with respect to this paper, to Deposit Account No. 01-2340.

Respectfully submitted,

ARMSTRONG, KRATZ, QUINTOS, HANSON & BROOKS, LLP



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Enclosures: Exhibit B

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